

10062952

ILE 'HOME' ENTERED AT 11:24:38 ON 20 SEP 2003

=> file biosis caplus medline embase

COST IN U.S. DOLLARS

SINCE FILE

ENTRY

TOTAL

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'BIOSIS' ENTERED AT 11:25:19 ON 20 SEP 2003

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FILE 'CAPLUS' ENTERED AT 11:25:19 ON 20 SEP 2003

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FILE 'MEDLINE' ENTERED AT 11:25:19 ON 20 SEP 2003

FILE 'EMBASE' ENTERED AT 11:25:19 ON 20 SEP 2003

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=> s ribonucleotide1(10a)alkyl

1(10A)ALKYL IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.

For a list of commands available to you in the current file, enter

"HELP COMMANDS" at an arrow prompt (>).

=>.s ribonucleotide#(10a)alkyl

L1 21 RIBONUCLEOTIDE#(10A) ALKYL

=> s l1 and polymerase# and reverse transcriptase#

L2 0 L1 AND POLYMERASE# AND REVERSE TRANSCRIPTASE#

=> s l1 anad polymerase#

MISSING OPERATOR L1 ANAD

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> s l1 and polymerase#

L3 3 L1 AND POLYMERASE#

=> s l3 and reverse transcriptase#

L4 0 L3 AND REVERSE TRANSCRIPTASE#

=> s l3 and (composition# or kit#)

L5 0 L3 AND (COMPOSITION# OR KIT#)

=> dup rem l3

PROCESSING COMPLETED FOR L3

L6 3 DUP REM L3 (0 DUPLICATES REMOVED)

=> d 16 1-3 bib ab kwic

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1999:72676 CAPLUS

DN 130:204673

TI Cytotoxicity of substituted alkyl-3,4-bis(4-methoxyphenyl)pyrrole-2-carboxylates in L1210 lymphoid leukemia cells

AU Burnham, Bruce S.; Gupton, John T.; Krumpe, Keith; Webb, T.; Shuford, Jordan; Bowers, Brook; Warren, Amy E.; Barnes, Cheryl; Hall, Iris H.

CS Department Chemistry, University North Carolina, Asheville, NC, 28804, USA

SO Archiv der Pharmazie (Weinheim, Germany) (1998), 331(11), 337-341

CODEN: ARPMAS; ISSN: 0365-6233

PB Wiley-VCH Verlag GmbH

DT Journal

LA English  
AB Two alkyl-3,4-bis(4-methoxyphenyl)pyrrole-2-carboxylates proved to be potent cytotoxic agents in the murine L1210 lymphoid leukemia screen. DNA synthesis was preferentially inhibited with the major target of the agents being de novo purine biosynthesis at the regulatory enzyme sites of PRPP-amido transferase and IMP dehydrogenase. Other enzymic activities which were suppressed by the drugs were DNA **polymerase .alpha.**, RNA **polymerases**, ribonucleoside reductase, and dihydrofolate reductase. The d[NTP] pools, nucleoside kinase, and the pyrimidine pathway were not affected by the presence of drugs. The DNA mol. itself was not the target of the agents, i.e. no alkylation of nucleotide bases, intercalation between bases or crosslinking of DNA strands occurred. The agents did cause L1210 DNA fragmentation after 24 h incubation at 100 .mu.M.

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Two alkyl-3,4-bis(4-methoxyphenyl)pyrrole-2-carboxylates proved to be potent cytotoxic agents in the murine L1210 lymphoid leukemia screen. DNA synthesis was preferentially inhibited with the major target of the agents being de novo purine biosynthesis at the regulatory enzyme sites of PRPP-amido transferase and IMP dehydrogenase. Other enzymic activities which were suppressed by the drugs were DNA **polymerase .alpha.**, RNA **polymerases**, ribonucleoside reductase, and dihydrofolate reductase. The d[NTP] pools, nucleoside kinase, and the pyrimidine pathway were not affected by the presence of drugs. The DNA mol. itself was not the target of the agents, i.e. no alkylation of nucleotide bases, intercalation between bases or crosslinking of DNA strands occurred. The agents did cause L1210 DNA fragmentation after 24 h incubation at 100 .mu.M.

IT 2056-98-6, d[CTP] 9002-03-3, Dihydrofolate reductase 9014-24-8, RNA **polymerase** 9014-43-1, Thymidine monophosphate kinase 9026-11-3, TRNA **Polymerase** 9028-93-7, IMP dehydrogenase 9031-61-2, Thymidylate synthase 9031-82-7, PRPP amido transferase 9040-57-7, **Ribonucleotide** reductase  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)  
(cytotoxicity of substituted **alkyl-3,4-bis(4-methoxyphenyl)pyrrole-2-carboxylates** in L1210 lymphoid leukemia cells)

IT 9012-90-2, DNA **polymerase**  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)  
(.alpha.; cytotoxicity of substituted **alkyl-3,4-bis(4-methoxyphenyl)pyrrole-2-carboxylates** in L1210 lymphoid leukemia cells)

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1995:435364 CAPLUS

DN 122:204573

TI Cytotoxicity of imides-N-alkyl semicarbazones, thiosemicarbazones, acetylhydrazones and related derivatives

AU Hall, Iris H.; Wong, OT; Chapman, James M.

CS Division of Medicinal Chemistry & Natural Products, Univ. of North Carolina at Chapel Hill, Chapel Hill, NC, 27599, USA

SO Anti-Cancer Drugs (1995), 6(1), 147-53

CODEN: ANTDEV; ISSN: 0959-4973

PB Rapid Science Publishers

DT Journal

LA English

AB The semicarbazones, thiosemicarbazones and acetyl-hydrazones of phthalimide, o-benzosulfimide, naphthalimide and diphenimide demonstrated potent cytotoxicity against murine and human leukemia cell growth and cultured cell growth from human solid tumors. The major site of inhibition in L210 leukemia cells was DNA synthesis after 60 min incubated with the agents at 25, 50 and 100 .mu.M. De novo synthesis of purines at the regulatory enzymes sites of PRPP amidotransferase and IMP

dehydrogenase were the major targets of the agent. Thymidylate synthetase, dihydrofolate reductase and ribonucleoside reductase activities were inhibited by the agents in a manner which would contribute to the overall redn. of DNA synthesis and cell death. D(NTP) pools were significantly reduced and the evidence suggests that the agents interacted with DNA affording DNA strand scission which would interfere with both template utilization by the **polymerases** and also ultimately reduce nucleic acid synthesis.

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IT 9002-03-3, Dihydrofolate reductase 9028-93-7, IMP dehydrogenase  
 9031-61-2, Thymidylate synthetase 9031-82-7, PRPP amidotransferase  
 9047-64-7, **Ribonucleotide** reductase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (in cytotoxicity of imides-N-alkyl semicarbazones,  
 thiosemicarbazones, acetylhydrazone and related derivs.)

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1990:235185 CAPLUS  
 DN 112:235185  
 TI Synergistic antiviral agents containing acyclic 2-aminopurine nucleosides and 2-acylpyridine hydrazone derivatives, ribonucleotide reductase inhibitors  
 IN Blumenkopf, Todd Andrew; Spector, Thomas; Averett, Devron Randolph; Morrison, Robert William, Jr.; Bigham, Eric Cleveland; Styles, Virgil Lee  
 PA Wellcome Foundation Ltd., UK  
 SO Eur. Pat. Appl., 34 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 349243	A2	19900103	EP 1989-306468	19890626
	EP 349243	A3	19900711		
	EP 349243	B1	19920401		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	DK 8903158	A	19891228	DK 1989-3158	19890626
	FI 8903112	A	19891228	FI 1989-3112	19890626
	AU 8937026	A1	19900201	AU 1989-37026	19890626
	AU 626304	B2	19920730		
	JP 02045423	A2	19900215	JP 1989-163628	19890626
	HU 52379	A2	19900728	HU 1989-3218	19890626
	HU 206264	B	19921028		
	ZA 8904835	A	19910227	ZA 1989-4835	19890626
	US 5021437	A	19910604	US 1989-371877	19890626
	AT 74276	E	19920415	AT 1989-306468	19890626
	ES 2031357	T3	19921201	ES 1989-306468	19890626
	US 5175165	A	19921229	US 1989-371482	19890626
	US 5164395	A	19921117	US 1991-663585	19910301
	US 5393883	A	19950228	US 1992-832228	19920207

US 5405850	A	19950411	US 1992-968270	19921029
PRAI GB 1988-15241		19880627		
EP 1989-306468		19890626		
US 1989-371482		19890626		
US 1989-371877		19890626		
US 1991-663585		19910301		
OS MARPAT 112:235185				
AB	<p>A combination of (1) an antiviral compd., e.g. (I; X = O, S; R = H, OH, NH<sub>2</sub>; Y = H, HOCH<sub>2</sub>) which can be converted in vivo to an inhibitor of or an alternative substrate for viral DNA polymerase via a metabolic pathway involving a step dependent upon a virus-induced enzyme and (2) a ribonucleotide reductase inhibitor [II; R<sub>1</sub>, R<sub>2</sub>, R<sub>4</sub>, R<sub>5</sub> = H, C<sub>1-6</sub> alkyl; R<sub>3</sub> = C(S)NR<sub>4</sub>NR<sub>5</sub>C(:X)NHR<sub>6</sub>, Q; R<sub>6</sub> = heterocyclyl C<sub>1-6</sub> alkyl, adamantyl, aryl C<sub>1-6</sub> alkyl, aroyl, aryl, etc.; R<sub>7</sub> = NHR<sub>6</sub>, 2-oxo or -thiobenzimidazolidin-1-yl, SH, C<sub>1-6</sub> alkylthio] (prepn. given) has a synergistic antiviral effect and is useful for the treatment or prophylaxis of a herpes viral infection in the human or animal body. Thus, condensation of 2-acetylpyridine with thiocarbohydrazide in MeOH under reflux gave 97% 2-acetylpyridine thiocarbonohydrazone which was acylated with 2-ClC<sub>6</sub>H<sub>4</sub>NCS in DMF to give II [R<sub>1</sub> = H, R<sub>2</sub> = Me, R<sub>3</sub> = C(S)NHC<sub>6</sub>H<sub>4</sub>Cl-2] (III). The presence of 1.3 .mu.M III in vitro increased 8.4 fold the potency of acyclovir for inhibiting herpes simplex virus. A tablet, capsule, and 2 cream formulations contg. I (R<sub>1</sub> = H, R<sub>2</sub> = Me, R<sub>3</sub> = 4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl) and acyclovir were prep'd.</p>			
AB	<p>A combination of (1) an antiviral compd., e.g. (I; X = O, S; R = H, OH, NH<sub>2</sub>; Y = H, HOCH<sub>2</sub>) which can be converted in vivo to an inhibitor of or an alternative substrate for viral DNA polymerase via a metabolic pathway involving a step dependent upon a virus-induced enzyme and (2) a ribonucleotide reductase inhibitor [II; R<sub>1</sub>, R<sub>2</sub>, R<sub>4</sub>, R<sub>5</sub> = H, C<sub>1-6</sub> alkyl; R<sub>3</sub> = C(S)NR<sub>4</sub>NR<sub>5</sub>C(:X)NHR<sub>6</sub>, Q; R<sub>6</sub> = heterocyclyl C<sub>1-6</sub> alkyl, adamantyl, aryl C<sub>1-6</sub> alkyl, aroyl, aryl, etc.; R<sub>7</sub> = NHR<sub>6</sub>, 2-oxo or -thiobenzimidazolidin-1-yl, SH, C<sub>1-6</sub> alkylthio] (prepn. given) has a synergistic antiviral effect and is useful for the treatment or prophylaxis of a herpes viral infection in the human or animal body. Thus, condensation of 2-acetylpyridine with thiocarbohydrazide in MeOH under reflux gave 97% 2-acetylpyridine thiocarbonohydrazone which was acylated with 2-ClC<sub>6</sub>H<sub>4</sub>NCS in DMF to give II [R<sub>1</sub> = H, R<sub>2</sub> = Me, R<sub>3</sub> = C(S)NHC<sub>6</sub>H<sub>4</sub>Cl-2] (III). The presence of 1.3 .mu.M III in vitro increased 8.4 fold the potency of acyclovir for inhibiting herpes simplex virus. A tablet, capsule, and 2 cream formulations contg. I (R<sub>1</sub> = H, R<sub>2</sub> = Me, R<sub>3</sub> = 4,5-dihydro-5-thioxo-1,3,4-thiadiazol-2-yl) and acyclovir were prep'd.</p>			

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